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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/730,329	12/04/2000	Varghese John	00228-US-NEW3	8197

20350 7590 06/27/2005

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EXAMINER

KAM, CHIH MIN

ART UNIT PAPER NUMBER

1653

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	09/730,329	JOHN ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2005.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 11-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

5.0-2

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group I, claims 1-14, formula I in the reply filed on April 21, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 11-14 directed to formula II, and claims 15-21 are non-elected invention and withdrawn from consideration. Therefore, claims 1-10 and formula I are examined.
2. A preliminary amendment filed June 21, 2004 is acknowledged. In the amendment, a paper copy of sequence listing, CRF and a statement indicating the paper copy and the CRF are the same has been submitted, and CRF has been entered; a substituted specification with deletion of the drawings and addition of sequence identifiers (SEQ ID NO:) has been submitted and entered; and claims 1, 2, 5-7, 10-16 and 19-21 have been amended.

### ***Informalities***

The disclosure is objected to because of the following informalities:

3. The specification cites Fig. 11 in paragraph [0107] (page 29) and Fig. 4 in paragraph [0200] (page 61), although Figs. 4 and 11 no longer exist. Appropriate correction is required.
4. The specification cites the cloning vector pCEK2 at page 58, however, the map is too small to read and covered by unrelated characters. Appropriate correction is required.
5. The specification cites the IC<sub>50</sub> values in "μm", which is not proper because the value should be cited as "μM", if the unit is micromolar. Appropriate clarification is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
- The specification is not enabling for a crystalline protein composition containing a  $\beta$ -secretase inhibitor molecule of formula I because the specification only discloses cursory conclusions without data supporting the findings, which state that the present invention is directed to a crystalline protein composition formed from a purified  $\beta$ -secretase protein, including a composition where the purified protein is characterized by an ability to bind to the  $\beta$ -secretase inhibitor substrate P 10-P4'sta D $\rightarrow$ V, also to a crystalline protein composition containing a  $\beta$ -secretase substrate or inhibitor molecule (paragraph [0007]). There are no indicia that the present application enables the claims in view of a crystalline protein composition containing a  $\beta$ -secretase inhibitor molecule of formula I as discussed in the stated rejection. The specification does not provide sufficient teachings on how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or

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unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding identities of the proteins in the crystalline protein composition containing a  $\beta$ -secretase inhibitor molecule of formula I, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification indicates purification of  $\beta$ -secretase (Example 5); and the preparation of P10-P4'sta(D $\rightarrow$ V) Sepharose Affinity Matrix and synthesis of heptamer peptides (compounds of formula I), where heptamer peptides inhibit activities of  $\beta$ -secretase (Example 7). However, there are no working examples indicating the formation and isolation of a crystalline protein composition comprising a specific protein (e.g.,  $\beta$ -secretase) and an inhibitor of formula I, the specification has not demonstrated a crystalline protein composition containing a bound inhibitor.

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., U.S. Patent 5, 744,346; paragraph [0004]) indicates the initial isolation and partial purification of  $\beta$ -secretase; and U.S. Patent 5,175,298 relates to the synthesis and use of hydroxyethylene isosteres as protease inhibitors (paragraph [0005]). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide teachings on identities of various proteins in the crystalline protein composition containing a  $\beta$ -secretase inhibitor molecule of formula I, where the formation of protein-inhibitor complex is needed.

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(4). Predictability or unpredictability of the art:

The claim encompasses a crystalline protein composition containing a  $\beta$ -secretase inhibitor molecule of formula I. Although the process for crystallization of protein and inhibitor such as co-crystallization or soaking experiment has been indicated, the crystalline protein composition (e.g.,  $\beta$ -secretase) containing an inhibitor ligand such as P10-P4'sta(D $\rightarrow$ V) or an inhibitor of formula I has not been demonstrated (paragraphs [0105] and [0106]). Since the specification does not provide sufficient teachings on identities of proteins used for forming crystalline structure with the inhibitor of formula I, and the binding activity of the inhibitor to the protein, the effect of forming protein-inhibitor crystals is unpredictable.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claim is directed to a crystalline protein composition containing a  $\beta$ -secretase inhibitor molecule of formula I. The specification indicates purification of  $\beta$ -secretase (Example 5); and the preparation of P10-P4'sta(D $\rightarrow$ V) Sepharose Affinity Matrix and synthesis of heptamer peptides (compounds of formula I), where the heptamer peptides inhibit the activities of  $\beta$ -secretase (Example 7). However, the specification has not demonstrated a crystalline composition comprising a specific protein with a bound inhibitor of formula I. Furthermore, there are no working examples indicating the formation and isolation of a crystalline protein composition comprising a specific protein and an inhibitor of formula I. Since the specification fails to provide sufficient teachings on identities of proteins that form crystalline structures with an inhibitor of formula I and the binding activity of the inhibitor to the protein, it is necessary to

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carry out further undue experimentation to assess the formation of a crystalline composition using various proteins and an inhibitor of formula I.

(6). Nature of the Invention

The scope of the claim encompasses a crystalline protein composition containing a  $\beta$ -secretase inhibitor molecule of formula I, but the specification does not provide sufficient teaching on the formation of a crystalline composition using a protein and an inhibitor of formula I. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, there is no working example demonstrating the claimed composition, the teachings in the specification are limited, and the formation of the crystalline protein composition is unpredictable, and therefore, it is necessary to carry out further experimentation to assess the formation of the protein crystalline composition.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-10 are indefinite because the claim recites the term "V, A, E, and F are valine, alanine, glutamine and phenylalanine respectively including conservative substituents thereof". The cited term renders the claim indefinite, it is not clear how "V, A, E, and F" can be also conservative substituents since the amino acid residues of formula I at positions 1, 5, 6 and 7 are defined as valine, alanine, glutamine and phenylalanine, respectively. Claims 2-5 and 7-10 are

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included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

***Conclusion***

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.  
Patent Examiner



**CHIH-MIN KAM  
PATENT EXAMINER**

CMK  
June 21, 2005